STEPHEN S. RABINOWITZ
srabinowitz@friedfrank.com
RANDY C. EISENSMITH (*Pro Hac Vice)*
randy.eisensmith@friedfrank.com
FRIED, FRANK, HARRIS, SHRIVER
& JACOBSON LLP
ONE NEW YORK PLAZA
NEW YORK, NEW YORK 10001
Telephone: 212-859-8000
Facsimile: 212-859-4000

DURIE TANGRI LLP
DARALYN J. DURIE (SBN 169825)
ddurie@durietangri.com
JOSHUA H. LERNER (SBN 220755)
jlerner@durietangri.com
GENEVIEVE P. ROSLOFF (SBN 258234)
grosloff@durietangri.com
217 Leidesdorff Street
San Francisco, CA 94111
Telephone: 415-362-6666
Facsimile: 415-236-6300

Attorneys for Plaintiffs
GENENTECH, INC. and
ROCHE PALO ALTO LLC

UNITED STATES DISTRICT COURT

FOR THE NORTHERN DISTRICT OF CALIFORNIA

GENENTECH, INC. and
ROCHE PALO ALTO LLC,

Plaintiffs,

v.

SANDOZ INC.

Defendant.

Case No. 3:11-cv-01925-JSW
Related Case No. 3:11-cv-02410-JSW

PLAINTIFFS' OPENING CLAIM CONSTRUCTION BRIEF

Date: April 10, 2012 at 1:30 p.m.
Ctrm: 11, 19th Floor
Judge: Honorable Jeffrey S. White

TABLE OF CONTENTS

TABLE OF AUTHORITIES

Page(s)

CASES

OTHER AUTHORITIES

I. INTRODUCTION

This is a Hatch-Waxman patent action for infringement of U.S. Patent No. 6,083,953 ("the '953 patent"), which protects the prescription drug VALCYTE® and methods for treating a person infected with cytomegalovirus. The parties dispute the meaning of one phrase ("in crystalline form") that appears in claim 1 of the '953 patent. As set forth below, Plaintiffs Genentech, Inc. ("Genentech") and Roche Palo Alto LLC ("Roche Palo Alto") ask the Court to construe this term in accordance with its ordinary and customary meaning to persons skilled in the art in view of the '953 patent specification. Plaintiffs' proposed construction of the term "in crystalline form" as used in claim 1 of the '953 patent is identical to that recently adopted by the United States District Court for the District of Delaware for the same term in the same patent claim. Defendant Sandoz Inc. ("Sandoz"), on the other hand, asks the Court to adopt a "construction" that would insert extraneous and wholly new limitations into claim 1 of the '953 patent. Plaintiffs respectfully submit that, under applicable Federal Circuit precedent, Sandoz's proposed claim construction is improper, and that the Court should construe the disputed claim term as having the meaning set forth in Plaintiffs' portion of the Joint Claim Construction and Prehearing Statement filed with the Court on November 28, 2011 (Docket No. 52).

II. NATURE AND STAGE OF THE PROCEEDINGS

Roche Palo Alto is the owner of the '953 patent and the holder of approved New Drug Application ("NDA") No. 21-304 for VALCYTE® 450 mg tablets, which contain the active ingredient valganciclovir hydrochloride. The '953 patent is listed in the FDA publication "Approved Drug Products With Therapeutic Equivalence Evaluations" (commonly known as the "Orange Book") in connection with Roche's VALCYTE® 450 mg tablets, a medication that is taken orally.

Roche Palo Alto commenced this action on April 20, 2011, after receiving notice that Sandoz had filed ANDA No. 202575 seeking approval to market generic valganciclovir hydrochloride 450 mg tablets and had made a "Paragraph IV Certification" against the '953 patent. Complaint ¶¶ 9-10 (Docket No. 6; copy submitted as Rabinowitz Declaration, Exh. 1). In its notice, Sandoz contended that use of its

proposed product would not infringe the '953 patent because the active ingredient in its product (valganciclovir hydrochloride) supposedly exists in "amorphous" rather than "crystalline" form at the time of its manufacture and shipment to wholesale or retail distributors. *See id.* ¶ 10. Plaintiffs contend that the valganciclovir hydrochloride in Sandoz's proposed product will comprise or convert to crystalline form at least during use by patients, e.g., upon exposure to ambient atmospheric humidity during storage in pill trays. *Id.* ¶ 16.

Discovery in this case is under way in accordance with a Court-approved scheduling order. *See* Docket Nos. 41 (Joint Case Management Statement) and 44 (Minute Order dated July 29, 2011). On November 28, 2011, the parties filed a Joint Claim Construction and Prehearing Statement that included claim charts setting forth their agreed and disputed claim constructions. Docket No. 52 at 2. A claim construction tutorial has been scheduled by the Court for April 3, 2012, and a claim construction hearing has been scheduled for April 10, 2012. Clerk's Notice dated August 1, 2011 (Docket No. 45).

III. BACKGROUND AND OVERVIEW OF THE TECHNOLOGY

A. Cytomegalovirus Infection in Patients with Immune Deficiency

Patients with immune deficiency, including recipients of certain organ transplants and patients with advanced HIV infection, are susceptible to infection by viruses such as cytomegalovirus ("CMV") with potentially devastating consequences, including blindness or death. Prior to the invention of the '953 patent, ganciclovir was the leading drug for treating such infections. '953 patent at col. 5, lines 47-52 (Rabinowitz Decl., Exh. 2). However, ganciclovir has very limited bioavailability when given orally, and must frequently be given intravenously or by injection directly into the eye. *Id.* Accordingly, there was an urgent need for a drug with the therapeutic efficacy of ganciclovir but with improved bioavailability when given orally. *Id.*

B. The Patented Invention: A Prodrug of Ganciclovir with Improved Oral Absorption and Low Toxicity

The inventors of the '953 patent made a novel chemical compound that consists of one molecule of ganciclovir joined by a particular chemical bond (called an "ester linkage") to one molecule of a particular amino acid (L-valine).[1] The inventors showed that the hydrochloride salt of this novel compound can be obtained in crystalline form, (*id*. at col. 23, line 18 to col. 24, line 8), and that it can be used as a prodrug of ganciclovir because it is well absorbed orally, is non-toxic, and upon absorption is metabolized so as to liberate ganciclovir in the bloodstream. (*Id*. at col. 27, line 35 to col. 29, line 33). The commercial embodiment of the invention is marketed as VALCYTE® and provides a safe and effective oral therapy for treatment of CMV infection in immuno-compromised patients.

IV. LEGAL STANDARDS FOR CLAIM CONSTRUCTION

Claim construction is a matter exclusively for the Court. *Markman v. Westview Instruments, Inc.*, 517 U.S. 370, 391 (1996). The Federal Circuit, following the Supreme Court's opinion in *Markman*, has established legal principles for ascertaining the proper meaning and scope of patent claim terms.

A. Claim Terms Are Presumed to Have Their Ordinary Meaning

"'In construing claims, the analytical focus must begin and remain centered on the language of the claims themselves, for it is that language that the patentee chose to use to particularly point out and distinctly claim the subject matter which the patentee regards as his invention.'" *Gillette Co. v. Energizer Holdings, Inc.*, 405 F.3d 1367, 1370 (Fed. Cir. 2005) (quoting *Interactive Gift Express, Inc. v. Compuserve, Inc.*, 256 F.3d 1323, 1331 (Fed. Cir. 2001)).

The words used by the patentee to claim his invention are presumed to have their ordinary and customary meaning. *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312 (Fed. Cir. 2005) (en banc) ("We have

[1] Ganciclovir has two free hydroxyl groups, each of which is capable of forming an ester linkage with another molecule. The compound claimed in the '953 patent has a single ester linkage and accordingly is called a **mono**-ester. A compound having **two** ester linkages is called a **bis**-ester. The compound claimed in the '953 patent also contains just one molecule of L-valine ("L" in this context denoting a **left-handed form** of a chiral molecule), and accordingly is called a **mono**-valinate. A compound containing two molecules of valine is called a **bis**-valinate.

frequently stated that the words of a claim 'are generally given their ordinary and customary meaning.'") (quoting *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1582 (Fed. Cir. 1996)); *Fuji Photo Film Co., Ltd. v. Int'l Trade Comm'n*, 386 F.3d 1095, 1105 (Fed. Cir. 2004) (noting that an accused infringer cannot overcome the heavy presumption that claims should be given their ordinary meaning simply by pointing to the preferred embodiment or other structures or steps disclosed in the specification).

Accordingly, "the claim construction inquiry . . . begins and ends in all cases with the actual words of the claim." *Teleflex, Inc. v. Ficosa N. Am. Corp.*, 299 F.3d 1313, 1324 (Fed. Cir. 2002) (quoting *Renishaw PLC v. Marposs Societa' per Azioni*, 158 F.3d 1243, 1248 (Fed. Cir. 1998)). "Dictionaries or comparable sources are often useful to assist in understanding the commonly understood meaning of words and have been used both by our court and the Supreme Court in claim interpretation." *Phillips*, 415 F.3d at 1322. Although such a source technically falls within the category of extrinsic evidence, it has "the value of being an unbiased source 'accessible to the public in advance of litigation.'" *Id.* (quoting *Vitronics*, 90 F.3d at 1585). "[J]udges are free to consult dictionaries and technical treatises 'at any time in order to better understand the underlying technology and may also rely on dictionary definitions when construing claim terms, so long as the dictionary definition does not contradict any definition found in or ascertained by a reading of the patent documents.'" *Phillips*, 415 F.3d at 1322-23 (quoting *Vitronics*, 90 F.3d at 1584 n.6).

B. The Scope of a Claim Term May Not Be Limited by Reading in Extraneous Limitations From the Specification

While claim terms must be interpreted in light of the specification, it is "one of the cardinal sins of patent law" to read a limitation from the written description into the claims. *Phillips*, 415 F.3d at 1320 (quoting *SciMed Life Sys., Inc. v. Advanced Cardiovascular Sys., Inc.*, 242 F.3d 1337, 1340 (Fed. Cir. 2001)). The rule against importing limitations into claims is succinctly explained as follows: "If everything in the specification were required to be read into the claims, or if structural claims were to be limited to devices operated precisely as a specification-described embodiment is operated, there would be

no need for claims." *Teleflex*, 299 F.3d at 1326 (quoting *SRI Int'l v. Matsushita Elec. Corp. of Am.*, 775 F.2d 1107, 1121 (Fed. Cir. 1985)(en banc) (plurality opinion)). In order to discern "the line between construing terms and importing limitations . . . the court's focus [should] remain[] on understanding how a person of ordinary skill in the art would understand the claim terms." *Phillips*, 415 F.3d at 1323. "[A]lthough the specification often describes very specific embodiments of the invention, we have repeatedly warned against confining the claims to those embodiments." *Id.*

Patentees are not required to include within each of their claims all of the advantages or features described as significant or important in the written description. *Golight, Inc. v. Wal-Mart Stores, Inc.*, 355 F.3d 1327, 1331-32 (Fed. Cir. 2004). This is so because "[a]n invention may possess a number of advantages or purposes, and there is no requirement that every claim directed to that invention be limited to encompass all of them." *E-Pass Techs., Inc. v. 3Com Corp.*, 343 F.3d 1364, 1370 (Fed. Cir. 2003). Similarly, "[a]n applicant is not necessarily required by 35 U.S.C. § 112, ¶ 1, to describe more embodiments than its preferred one, and [the Federal Circuit has] outright rejected the notion that disclosure of a single embodiment necessarily limits the claims." *Golight*, 355 F.3d at 1331; *see also Phillips*, 415 F.3d at 1323 ("[W]e have expressly rejected the contention that if a patent describes only a single embodiment, the claims of the patent must be construed as being limited to that embodiment."); *Teleflex*, 299 F.3d at 1327 (stating that "the number of embodiments disclosed in the specification is not determinative of the meaning of disputed claim terms").

Thus, "particular embodiments appearing in the written description will not be used to limit claim language that has broader effect." *Innova/Pure Water, Inc. v. Safari Water Filtration Sys., Inc.*, 381 F.3d 1111, 1117 (Fed. Cir. 2004). Moreover, "'[a] claim interpretation that excludes a preferred embodiment from the scope of the claim is rarely, if ever, correct.'" *Verizon Servs. Corp. v. Vonage Holdings Corp.*, 503 F.3d 1295, 1305 (Fed. Cir. 2007) (quoting *MBO Labs., Inc. v. Becton, Dickinson & Co.*, 474 F.3d 1323, 1333 (Fed. Cir. 2007)) (internal citation omitted in original); *accord Adams Respiratory*

Therapeutics, Inc v. Perrigo Co., 616 F.3d 1283, 1290 (Fed. Cir. 2010) (quoting *Vitronics*, 90 F.3d at 1583).

C. Any Alleged Disavowal of the Ordinary Meaning From the Prosecution History or Patent Specification Must Be Clear and Unequivocal

Regardless of the number of ways or detail with which features are described in the specification of a patent, the Federal Circuit has circumscribed the ways in which a court may constrict the ordinary meaning of a claim term, based on either the patent specification or prosecution history. As to the specification, the written description may only be used to restrict the scope of the claims if "the patentee demonstrated an intent to deviate from the ordinary and accustomed meaning of a claim term by redefining the term or by characterizing the invention in the intrinsic record using words or expressions of manifest exclusion or restriction, representing a clear disavowal of claim scope." *Teleflex*, 299 F.3d at 1327; *see also Phillips*, 415 F.3d at 1316 ("[T]he specification may reveal an intentional disclaimer, or disavowal, of claim scope by the inventor. In that instance . . . the inventor has dictated the correct claim scope, and the inventor's intention, as expressed in the specification, is regarded as dispositive."). The patent's written description may not be used to narrow the scope of the claimed invention absent a clear disclaimer. *Brookhill-Wilk 1, LLC v. Intuitive Surgical, Inc.*, 334 F.3d 1294, 1301 (Fed. Cir. 2003) ("Absent a clear disclaimer of particular subject matter, the fact that the inventor anticipated that the invention may be used in a particular manner does not limit the scope to that narrow context."). In short, the presumption in favor of the broad construction of a claim term will only be overcome where the patentee, acting as his or her own lexicographer, has clearly set forth an explicit definition of the term different from its ordinary meaning. *See In re Paulsen*, 30 F.3d 1475, 1480 (Fed. Cir. 1994); *Intellicall, Inc. v. Phonometrics, Inc.*, 952 F.2d 1384, 1387-88 (Fed. Cir. 1992).

As to the prosecution history, the Federal Circuit has consistently declined to find any disclaimer based on prosecution history unless the alleged disavowal of claim scope is "clear and unmistakable." *Omega Eng'g, Inc. v. Raytek Corp.*, 334 F.3d 1314, 1325-26 (Fed. Cir. 2003); *see also Phillips*, 415 F.3d

at 1317 ("because the prosecution history represents an ongoing negotiation between the PTO and the applicant, rather than the final product of that negotiation, it often lacks the clarity of the specification and thus is less useful for claim construction purposes."). If an alleged disclaimer is ambiguous, disavowal will not be found. *Omega Eng'g*, 334 F.3d at 1324 ("We have, however, declined to apply the doctrine of prosecution disclaimer where the alleged disavowal of claim scope is ambiguous."); *Rexnord Corp. v. The Laitram Corp.*, 274 F.3d 1336, 1347 (Fed. Cir. 2001) (refusing to limit the ordinary meaning of the claim because the alleged disclaimer in the file wrapper was at best "inconclusive"); *N. Telecom Ltd. v. Samsung Elecs. Co.*, 215 F.3d 1281, 1293-95 (Fed. Cir. 2000) (refusing to limit scope of claims where inventors' statements were amenable to multiple reasonable interpretations).

V. ARGUMENT

Claim 1 of the '953 patent reads as follows:

> The compound 2-(2-amino-1,6-dihydro-6-oxo-purin-9-yl)methoxy-3-hydroxy-1-propanyl-L-valinate hydrochloride **in crystalline form**.

'953 patent, col. 30, lines 42-44 (emphasis added).

The parties agree that the chemical name "2-(2-amino-1,6-dihydro-6-oxo-purin-9-yl)methoxy-3-hydroxy-1-propanyl-L-valinate hydrochloride" refers to the compound known as "valganciclovir hydrochloride." *See* Joint Claim Construction and Prehearing Statement (Docket No. 52) at 2. However, the parties dispute the meaning of the phrase "in crystalline form." *Id*.

For the reasons set forth below, the disputed phrase "in crystalline form" should be construed in accordance with its ordinary and accepted meaning in the scientific field of the '953 patent, consistent with its construction in concurrent litigation in the District of Delaware.

A. "In crystalline form" (claim 1)

Plaintiffs: in a physical form having molecules arranged in a regularly repeating three dimensional pattern. **Sandoz**: *prepared* in a *stable*, solid physical form having molecules arranged in a regularly repeating three dimensional pattern.

The specification does not include any definition of the phrase, "in crystalline form," which is generic and common in the art of pharmaceutical chemistry. "Crystalline" in this context is an adjective that characterizes the physical state of the claimed compound. Under the legal standards set forth above, the Court should construe the phrase "in crystalline form" as having its ordinary and customary meaning to a person skilled in the art of the '953 patent, the "art" here being pharmaceutical chemistry.

An authoritative text in the field of pharmaceutical chemistry, Remington's Pharmaceutical Sciences, provides the following definition of the "crystalline state":

> Atoms and molecules tend to organize themselves into their most favorable thermodynamic state, which under certain conditions results in their appearance as crystals. **This form is characterized by a highly ordered arrangement of the molecules, associated with which is a three-dimensional periodicity. The repeating three-dimensional patterns**, ideally depicted as lattices, are essential for X-ray structural analysis.

Remington's Pharmaceutical Sciences 172 (Alfonso R. Gennaro ed., 18th ed. 1990) (Rabinowitz Decl., Exh. 3) (emphasis added).

Other references, contemporaneous with the '953 patent, are to the same effect:

> There are two main classes of solids: crystalline and amorphous. What distinguishes them from one another is the nature of their atomic-scale structure. . . . Atomic positions in a crystal exhibit a property called long-range order or translational periodicity: positions repeat in space in a regular array . . . .

23 The New Encyclopaedia Britannica 637 (Encyclopaedia Britannica, Inc., 15th ed. 1994) (Rabinowitz Decl., Exh. 4).

The parties in fact agree that the claim calls for "a physical form [of the compound] having

molecules arranged in a regularly repeating three dimensional pattern." *See* Docket No. 52 at 2 (comparing Plaintiffs' and Sandoz's proposed constructions). However, Sandoz seeks to introduce additional limitations, which the Court should decline to adopt.

1. "*prepared* in a *stable*, solid physical form having molecules arranged in a regularly repeating three dimensional pattern"

Sandoz improperly seeks to import additional, extraneous limitations into the claim. Sandoz seeks to narrow the claim to require not only that the claimed compound *exist* in crystalline form (*i.e.*, "a physical form having molecules arranged in a regularly repeating three dimensional pattern"), but also that it must have been *prepared* in a specified manner and that it must be a *stable* solid physical form.[2]

Sandoz's proposed construction is at odds with the language of the claim, which does not recite any process step, but instead is directed to the claimed compound itself (valganciclovir hydrochloride in crystalline form) without regard to its method of preparation. Nor does the claim specify any requirement for stability. The fact that the specification discloses that this compound can, if desired, be used for manufacturing "stable oral formulations," (*see* '953 patent at col. 15, lines 7-9), is no basis for importing such a limitation into claim 1. *Brookhill-Wilk 1*, 334 F.3d at 1301 ("Absent a clear disclaimer of particular subject matter, the fact that the inventor anticipated that the invention may be used in a particular manner does not limit the scope to that narrow context."). Moreover, the fact that the specification discloses stability as one advantage of oral formulations containing the claimed compound does not justify importing such a limitation into this claim. As the Federal Circuit has warned: "Advantages described in the body of the specification, if not included in the claims, are not per se limitations to the claimed invention." *Brookhill-Wilk 1*, 334 F.3d at 1301; *accord Praxair, Inc. v. ATMI, Inc.*, 543 F.3d 1306, 1306 (Fed. Cir. 2008) ("An invention may possess a number of advantages or purposes, and there is no requirement that every claim directed to that invention be limited to encompass

[2] A "physical form having molecules arranged in a regularly repeating three dimensional pattern" is necessarily a solid rather than a liquid or a gas, so that the recitation of "solid" in Sandoz's proposed construction is redundant.

all of them.").

In construing claim 1 of the '953 patent in a Hatch-Waxman action, the U.S. District Court for the District of Delaware, adopted the construction proposed here by Plaintiffs and rejected the accused infringer's attempt to narrow the claim by importing extraneous limitations such as those proposed here by Sandoz. As Chief Judge Sleet explained:

> The court rejects Endo's proposed construction and adopts the plaintiff's proposed construction. Endo's proposed limitations [which include] "existing in a stable form when being processed into a pharmaceutical formulation" are not supported by the intrinsic record. . . . Adopting Endo's proposed construction thus would improperly import descriptions of preferred embodiments into the specification and impose them as limitations on the claims.

Roche Palo Alto LLC v. Endo Pharms., Inc., C.A. No. 10-261 (GMS), Order Construing the Terms of U.S. Patent No. 6,083,953 (D. Del. Aug. 11, 2011) at n.1 (copy attached as Rabinowitz Decl., Exh. 5).

VI. CONCLUSION

For the above reasons, and those to be stated in further briefing and in argument, Plaintiffs respectfully request that the Court adopt Plaintiffs' proposed construction of the disputed term, "in crystalline form."

Dated: January 12, 2012

STEPHEN S. RABINOWITZ
RANDY C. EISENSMITH
FRIED, FRANK, HARRIS, SHRIVER & JACOBSON LLP

DARALYN J. DURIE
JOSHUA H. LERNER
GENEVIEVE P. ROSLOFF
DURIE TANGRI LLP

By: */s/ Stephen S. Rabinowitz*
STEPHEN S. RABINOWITZ

Attorneys for Plaintiffs
GENENTECH, INC. and
ROCHE PALO ALTO LLC

8464926